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CORRESPONDENCE

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Comment to "Transplacental passage of a nonionic contrast agent"

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Sir: We read the article "transplacental passage of a nonionic contrast agent" by Vanhaesebrouck et al. [5] with interest. The authors present a case report and make statements in the discussion regarding the neural tolerance of the contrast agent used (iopromide, Ultravist). They state that iopromide is not indicated for intrathecal use and cite an article by Caillé and Allard [2] as the reference for such alleged severe reactions associated with the intrathecal use of iopromide.

We would like to comment on this:

There is considerable safety experience with this contrast agent. Since its launch in 1985 more than 90 million patients have been exposed to it, mostly with intravascular applications. However, iopromide (Ultravist 240) has also been investigated for the indication of myelography [1, 4] and has regulatory approval and is used in this indication in several countries. The article by Caillé and Allard [2] is not correctly cited in this context, as the nonionic monomers discussed do not include iopromide nor are any severe neurologic adverse reactions identified as related to its use. Regarding neural tolerance it is also worthy to mention that iopromide has been investigated, has regulatory approval and is widely used in cerebral angiography [3]. Also in this indication its neural tolerance has been shown to not differ from similar nonionic agents.

Yours sincerely,

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Letter to the editor

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CORRESPONDENCE

Piet Vanhaesebrouck

Comment to "Transplacental passage of a nonionic contrast agent"

Reply

Sir: We thank our colleagues Dr. Alexander Michel (Schering AG, Germany) and Dr. Ginette B. Jacob (Berlex Laboratories Inc, USA) for their comments on our paper "Transplacental passage of a nonionic contrast agent" [5].

The propositus who was the subject of the article under discussion was born 10 days following intravenous administration of iopromide (Ultravist) to his mother, and the nonionic contrast monomer was still detectable in the cerebral spinal fluid 9 days after birth. Therefore, we made a brief statement in the discussion regarding the potential neurotoxicity of the contrast agent used, as we could find repeated scientific information supplied by Schering AG or Berlex Inc. (an US affiliate of Schering AG, Germany) on the contraindication of iopromide for intrathecal use. Moreover, a paper by Wible et al. [6] reported severe neurotoxicity of non-ionic X-ray contrast media (iopromide and others) following intracisternal administration in a rat model that led to death, convulsions, apnea, hypoactivity and coma. Unfortunately this last reference was accidentally replaced by us during a revision procedure with the – in this context – non-relevant article by Caillé et al [1]. For this, we offer an apology to our correspondents and to the editor for this unintended reference mismatch.

However, with respect to the scientific safety information on the drug Ultravist we were confronted with contradictory data during our literature search. In the instruction leaflet supplied to date with the medication package by Schering AG in Belgium the indications for Ultravist 240, 300 and 370 are "contrast enhancement in computerized tomography (CT), digital subtraction angiography (DSA), intravenous urography, flebography, visualization of body cavities (e.g. arthrography, hysterosalpingography, fistulography) with the exception of myelography, ventriculography, cisternography" (sic) [3]. In the scientific leaflet "Ultravist Safety Information" updated in 2004 by Berlex Inc (USA) we also read: "Ultravist injection is not indicated for intrathecal use. Serious adverse reactions have been reported due to the inadvertent intrathecal administration of iodinated contrast media that are not indicated for intrathecal use. These serious adverse reactions include: death, convulsions, cerebral hemorrhage, coma, paralysis, arachnoiditis, acute renal failure, cardiac arrest, seizures, rhabdomyolysis, hyperthermia, and brain edema" (sic) [2]. Conversely, in the detailed drug prescribing information (updated in 2002) supplied by Schering AG, Germany, we still find a contradictory statement in relation to the diagnostic indications for Ultravist 240: "Contrast enhancement in computerized tomography (cranial CT), arteriography and venography including intraarterial digital subtraction angiography (DSA); intravenous urography, examination of the subarachnoid space and other body cavities (e.g. arthrography, hysterosalpingography)" (sic) [4].

On the basis of these statements, our correspondents should agree on the fact that depending on where the drug iopromide is supplied worldwide serious adverse reactions with intrathecal use are obviously interpreted inconsistently. It is generally assumed that regulatory approvals may differ from one country to another leading, for instance, to the approval of intrathecal use of iopromide in certain countries and not in others. Conversely, we propose that scientific safety information provided to the physician by pharmaceutical companies should be unequivocal and rigorously identical independent of the country in which the medication is prescribed. We fully agree with the manufacturer that it has not yet been sufficiently demonstrated that Ultravist is safe for use in pregnant patients.

Yours sincerely,

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